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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,251	11/01/2001	Robert K. Naviaux	UCSD1140-1	9760

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EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,251	NAVIAUX, ROBERT K.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67,70,73-81,84-91 and 95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *95* is/are allowed.

6)☒ Claim(s) *67,70,73-81 and 84-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's Response filed December 12, 2005 is acknowledged. Claims 82 and 83 are canceled. Claims 67, 70, 73-81, 84-91 and 95 remain under consideration.

The rejection of record under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to practice the invention, is withdrawn. Upon reconsideration of the prior art, this rejection directed to inadequate support for the breadth of the claimed subject matter is withdrawn. The prior art clearly teaches the administration of the prodrug triacetyluridine to treat a range of mitochondrial diseases.

Applicant's arguments with respect to claim67, 70 and 73-91 that were rejected in the last Office Action under 35 U.S.C. 103 as being unpatentable over Page et al., Proc. Natl. Acad. Sci., in view of von Borstel et al., U.S. Patent 6,472,378, have been considered but are moot in view of the new grounds of rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 67, 70, 73, 75-78, 80, 85, 89-91 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naviaux et al., a presentation at the "Mitochondrial Dysfunction in Human Pathology" meeting in Melbourne, Australia, 7 September, 1998.

Naviaux teaches the administration of triacetyluridine to treat and to reduce one or more symptoms associated with various mitochondrial disorders comprising administering triacetyluridine. Mitochondrial function is coupled to the enzyme

dihydroorotate dehydrogenase, as required by instant claims 76-78. Naviaux teaches the requirement for exogenous uridine by cells with mitochondrial dysfunction. The disorders specifically encompassed in the teaching are *inter alia* complex I deficiency, lactic academia, renal tubular acidosis, Leigh syndrome, mitochondrial myopathy, peripheral and autonomic neuropathy, gastrointestinal dysmotility, epilepsy and truncal ataxia. Improvement of symptoms was noted in all patients following administration of triacetyluridine. The claims differ in that the reference teaches the administration of triacetyluridine while the present claims require the administration of uridine or 1-β-D-ribofuranosyluracil. However, according to Naviaux, triacetyluridine is a prodrug of uridine that is rapidly converted to uridine by non-specific esterases in the gastrointestinal epithelium after oral administration. Triacetyluridine exhibits 5-10 times the bioavailability of uridine, permitting the achievement of therapeutic blood levels of uridine with substantially less drug. Therefore, in view of the teachings of the reference, clear motivation is provided to administer triacetyluridine with a reasonable expectation of achieving the same desired therapeutic outcome. Such would have been obvious because the prodrug provides greater bioavailability and is rapidly converted to uridine.

Claims 67, 70, 73, 75-81, 84-91 and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Page et al., Proc. Natl. Acad. Sci.

Page teaches the oral administration of uridine to treat a syndrome characterized by abnormal purine and pyrimidine metabolism. Dosage ranges are disclosed in column 2, page 11603. The patients presented with persistent hypouricosuria and decreased incorporation of uridine into nucleotides. Clinically, the patients exhibited

developmental delay, seizures, ataxia, recurrent infections, severe language deficit and an unusual behavioral phenotype characterized by hyperactivity, short attention span and poor social interaction. See Table 1, page 11602. Subsequent to uridine supplementation, according to Page, all patients showed remarkable improvement in speech and behavior. Multiple drug therapy in such disease states is conventional. Page suggests effects of increased nucleotide catabolism relates to the symptoms of these patients.

The claims differ in that Page does not use the term "mitochondrial disorder". However, Page uses the characterization "inborn error of metabolism" and teaches the same clinical presentations as those seen in patients with mitochondrial disorders. Further, because uridine administration has direct effects on the central nervous system, affords protection against γ-aminobutyric acid type A antagonist-induced seizures and demonstrates dopaminergic effects, it would have been reasonable to expect the metabolic basis for the effectiveness of oral uridine in the treatment of the developmental disorders described by Page are the same as those more recently termed mitochondrial disorders.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low can be reached on 591-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

Phyllis G. Spivack
Primary Examiner
Art Unit 1614

PHYLLIS SPIVACK
PRIMARY EXAMINER

March 6, 2006